

Amendments to Specification

Please replace the paragraph beginning at page 1, line 20, with the following amended paragraph:

Carotenoids having the above ~~described~~described features, include but not limited to, lutein, zeaxanthin, beta carotene and lycopene.

Please replace the paragraph beginning at page 2, line 10, with the following amended paragraph:

It has well been established that liposomes are suitable delivery vehicles for parenteral, peroral, topical and inhalation administration of drugs. Liposomes, which are biocompatible, may improve for an active substance the formulability, provide prolonged release, improve the therapeutic ~~ration~~ratio, prolong the therapeutic activity after each administration, reduce the need for frequent administration, reduce the amount of drug needed and/or absorbed by target tissue.

Please replace the paragraph beginning at page 3, line 2, with the following amended paragraph:

The present invention is based on a new method for preparing a bioavailable ~~formulations~~formulation containing water immiscible carotenoids.

**Please replace the paragraph beginning at page 3,
line 4, with the following amended paragraph:**

Thus, according to a first of its ~~aspects~~aspects, the present invention provides formulations comprising liposomes loaded with an amount of at least one carotenoid being immiscible in water.

**Please replace the paragraph beginning at page 3,
line 17, with the following amended paragraph:**

The term "**effective amount**" for the purposes described herein is that determined by such considerations as are known to those versed in the art. The amount of the carotenoids carried by the liposomes must be sufficient to achieve a desired therapeutic effect, e.g. to treat, prevent or ameliorate symptoms associated with a disease against which the carotenoids is effective, to lessen the severity or cure the disease or to prevent the disease from curingoccurring.

Particularly, the effective amount of the carotenoid is such that it acts against the harmful effects of undesired oxidation of lipids, proteins, tissues or cells, in the living body, for example, by environmental hazards, which can exert damage. Such environmental hazards include UV radiation or oxidative agents.

**Please replace the paragraph beginning at page 4,
line 21, with the following amended paragraph:**

The term "*liposome-forming lipids*" use herein refers to lipids, preferably amphipathic lipids which contain groups with charateristically different properties, e.g. both hydrophilic and hydrophobic properties, which upon dispersion thereof in an aqueous medium for vesicles (liposomes). The liposome-forming lipids may include a single type of lipids or a mixture of two or more lipids. The lipids may also be modified lipids, including PEGylated lipids an according to one preferred embodiment include unsaturated lipids.

**Please replace the paragraph beginning at page 6,
line 27, with the following amended paragraph:**

Other water-immiscible carotenoids which may be used in the formulation of the present invention include 4,4'-diketocarotenoid, astaxanthin, canthaxanthincanthaxanthin, zeaxanthin, beta-cryptoxanthin, lutein, 2',3'-anhydrolutein, B-carotene and rubixanthin, all of which are known to have scavenging and anti-oxidizing activity.

**Please replace the paragraph beginning at page 8,
line 5, with the following amended paragraph:**

Further, the formulation of the invention may also include other biologically functionally substances, such as vitamin A, vitamin E, etc.

**Please replace the paragraph beginning at page 8,
line 7, with the following amended paragraph:**

Yet further, the composition of the present invention may include a combination of one or more carotenoid and other antioxidants, such as vitamin C, vitamin E, beta ~~caroten~~-carotene (provitamin A), selenium, glutathione, cysteine, uric acid or synthetic antioxidant like DMSO, BHT, BHA and nitroxides. These additional anti-oxidants may either be entrapped in the lipid bilayer encapsulated within the liposome or be adhered to the surface of the liposome.

**Please replace the paragraph beginning at page 9,
line 24, with the following amended paragraph:**

(i) dissolving a powder of liposome-forming lipids in an organic solvent to a level close to saturation;

**Please replace the paragraph beginning at page 10,
line 4, with the following amended paragraph:**

(iii) dehydrating rehydrating the second dry powder in an aqueous solution to yield the carotenoid-containing liposomal formulations

**Please replace the paragraph beginning at page 12,
line 20, with the following amended paragraph:**

The following Table 1 summarizes the characterizing features of the materials employed in the following specific however, non-limiting, Examples. It should be noted that the commercial names of the substances used as liposome forming lipids indicate the percentage of

phosphatidylecholine phosphatidylcholine in the substance, e.g. S20 refers to 20% phosphatidylcholine in the mixture of lipids. In the same manner, S40 refers to 40%, S35 to 35% and E100 to 100% phosphatidylcholine in the mixture of lipids. The following examples, S20, S20N, S35, S40 and E100 are all products of Lipoid GmbH, Germany. The mixture of lipids in the liposomes forming lipids employed may include, in addition to the phosphatidylcholine, phosphatidyl ethanolamine, phosphatidyl inositol, or any other vesicle forming substances (e.g. oil, other lipids etc.).

**Please replace the paragraph beginning at page 14,
line 17, with the following amended paragraph:**

Lycopene Quantification-lycopene was analyzed for degradation and quantified by The HPLC buffer used comprised acetonitrile:methanol:methylene chloride:~~hexan~~hexane and a ratio of 850:100:25:25 (all HPLC grade, Hoffman La Roche). Quantification was based on a standard curve obtained for lycopene (~~Lycorad~~LycoRed standard ~~Please provide a referencee
from which this standard may be obtained~~). The amount of lycopene was also determined by absorbance at 472nm.

**Please replace the paragraph beginning at page 15,
line 10, with the following amended paragraph:**

Method of Preparation - The phospholipid phospholipids were dissolved in cyclohexane at a w/v ratio of 1 mg phospholipid per 10 ml cyclohexane. The dissolving required heating for several seconds at 60°C and /or sonication for up to 3 minutes. Lycopene was added as powder to the solution, which was then vortexed. The resulting solution was lyophilized overnight and kept at -20°C until use. To form multilamellar liposome (MLV), 2 ml of 0.9% NaCl were added to the lyophilizate followed by vortex to yield MLV encapsulated lycopene.

**Please replace the paragraph beginning at page 28,
line 4, with the following amended paragraph:**

As evident from the above results, the amount of lipids in the liposomal formulation did ~~no-not~~ substantially change with time while the amount of lycopene decreased with the formation of lycopene degradation products. The most stable powder was S03, meaning, liposomes composed of S45:lycopene 75% with weight ratio of 45:1, stored after lyophilization as a powder. Formulations S02 and S04 were less stable.